Version with markings to show changes made

In the specification:

Paragraph beginning at page 3, line 32, has been amended as follows:

Figure 2 is a compilation of graphical representations of data which indicate that [PS] pregnenolone sulfate (PS) inhibits [AMPA] α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA) and kainate receptor function. Figures [1(A)]2(A) through [1(D)]2D are representative traces showing the inhibitory effect of 100 μM PS on kainate-induced currents of oocytes injected with (A) rat brain poly(A)$^+$ RNA, (B) GluR1 cRNA, (C) GluR3 cRNA, (D) GluR6 cRNA. The kainate concentration used in (A)-(C) was 100 μM, and in (D) was 10 μM. The *solid bar* represents the period of kainate (KA) application; the *open bar* indicates the period of PS exposure. Figure [1(E)]2E is a graph of relative current for the indicated Kainate concentration. The administration of PS (open symbols) is seen to decreases maximum kainate responses of GluR1 (●, ○), GluR3 (■, □), and GluR6 (▲, Δ) receptors. Each *data point* represents the mean of three experiments. *Error bars* represent standard error. *Smooth curve* was determined by nonlinear regression using the logistic equation applied to pooled data. Fitted parameters are (GluR1) I_{max} =1.0, EC_{50}=27 μM, n_H=1.54; (GluR1 + PS) I_{max}=0.17, EC_{50}=23 μM, n_H=0.9; (GluR3) I_{max} =1.15, EC_{50}=27 μM, n_H=1.44; (GluR3 + PS) I_{max} =0.33, EC_{50}=32 μM, n_H=1.93; (GluR6) I_{max} =1.0, EC_{50}=550 nM, n_H=1.1; (GluR6 + PS) I_{max} =0.69, EC_{50}=570 nM, n_H=1.2. Figure [1(F)]2F is a graph of data showing the concentration dependence of PS inhibition of recombinant GluR1 (○), GluR3 (□), and GluR6 (▲) receptors. Results are expressed as percentage change in the peak 100 μM (GluR1 and GluR3) or 10 μM (GluR6) kainate-induced current in the presence of PS. Each *data point* is the mean of three experiments; *error bars* indicate S.E.M. For GluR1 and GluR3, *smooth curves* are derived from fits to the Michaelis-Menten equation, as fits to the logistic equation yielded Hill coefficients close to 1, with no significant improvement in sum of squares (F-test, $P > 0.05$). Fitted parameters are (GluR1) EC_{50}=43 μM, E_{max} = -99%; (GluR3) EC_{50}=12 μM, E_{max} = -90%. For GluR6, the smooth curve is derived from a fit to the logistic equation, as Michaelis-Menten fits were significantly poorer (F-test, $P < 0.05$). Maximum inhibition was constrained to 100%, as an

unconstrained fit yielded an extrapolated maximum inhibition >100%. Fitted parameters are EC_{50}=80 μM, n_H=0.29.

Paragraph beginning at page 5, line 4, has been amended as follows:

Figure 3 is a compilation of graphical representations of data which indicate that neuroactive steroids modulate NMDA responses of oocytes injected with specific NMDA receptor subunits. Figure [2(A)]3(A) indicates the potentiation of the 100 μM NMDA response by PS in oocytes injected with $NR1_{100}$ + NR2A cRNA. The *solid bar* indicates the period of NMDA exposure; the *open bar* indicates the period of PS exposure. Figure [2(B)]3(B) indicates inhibition of the 100 μM NMDA response by 3α5βS in oocytes injected with $NR1_{100}$ + NR2A cRNA. The s*olid bar* indicates the period of NMDA exposure; the *shaded bar* indicates the period of 3α5βS exposure. Figure [2(C)]3(C) indicates modulation of agonist efficacy by PS and 3α5βS in oocytes injected with $NR1_{100}$ + NR2A cRNA. PS (100 μM) increases the NMDA I_{max} but does not affect the EC_{50}. 3α5βS (100 μM) markedly reduces the NMDA I_{max} with little effect on EC_{50}. Peak NMDA responses are normalized to the peak 100 μM NMDA response. Each *data point* represents the mean of three experiments. *Error bars* represent standard error. *Smooth curves* are derived from fits to the logistic equation. Fitted parameters are (control) EC_{50}=29 μM, E_{max}=1.14, n_H=1.43; (+PS) EC_{50}=30 μM, E_{max}=3.21, n_H=1.54; (+3α5βS) EC_{50}=15 μM, E_{max}=0.35, n_H=1.66. Figure [2(D)]3(D) is a graph indicating the concentration dependence of steroid modulation of the NMDA response of oocytes injected with $NR1_{100}$ + NR2A cRNA. NMDA (100 μM) and the indicated concentration of PS (●), 3β5βS (Δ), or 3α5βS (□) were applied simultaneously for 10 s. The peak NMDA-induced current is expressed relative to the average of control NMDA responses determined before application of steroid and after steroid washout. *Points* indicate mean of 6 (PS and 3α5βS), and 4 (3β5βS), experiments. *Error bars* indicate S.E.M. Smooth curves are derived from fits to the Michaelis-Menten equation, as fits to the logistic equation yielded Hill coefficients close to 1, with no significant improvement in sum of squares (*F*-test, $P > 0.05$). Fitted parameters are (for PS) EC_{50}=32 μM, E_{max}=4.43 (for 3α5βS) EC_{50}=41 μM, E_{max}=0.1; (for 3β5βS) EC_{50}=79 μM, E_{max}=0.26. (E) Concentration dependence for PS enhancement (●) and 3α5βS (Δ) and 3β5βS (□) inhibition of the NMDA response of oocytes